

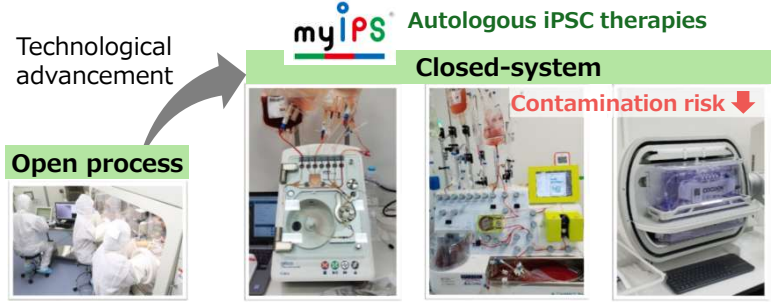
Development of a Sterility Assurance Model for Closed System Manufacturing in the "my iPS" Project

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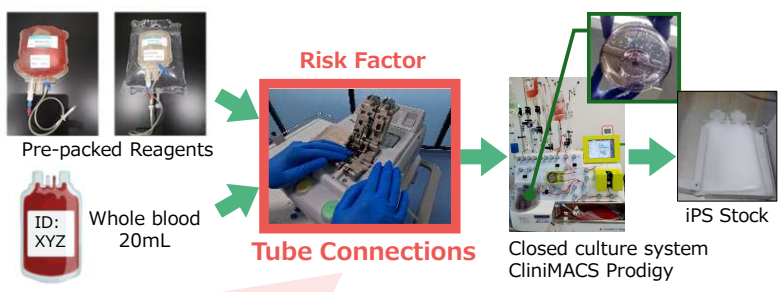


Introduction



- **Sterility assurance is essential** in both closed-system and open.
- Closed-system sterility assurance is not yet standardized.
- This study aims to develop a sterility assurance model for closed-system iPS manufacturing.

Target Process - Blood to iPS Closed System -



- Risk assessment identified several contamination-control factors (details omitted). **Tube connections were the highest-risk factor.**
- **→ We evaluated microbial contamination risks. Tube welding device vs Tube Connectors.**

Material & Methods

1. Tube welding device

Aseptic welding of tubing after artificial biofilm formation (ISO 4768 compliant) and high-microbial contamination on the outer surface.

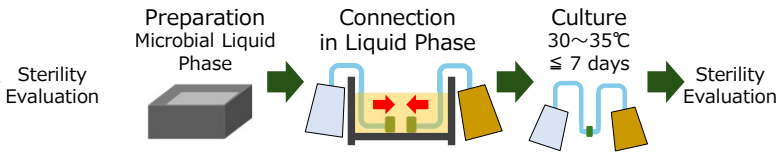
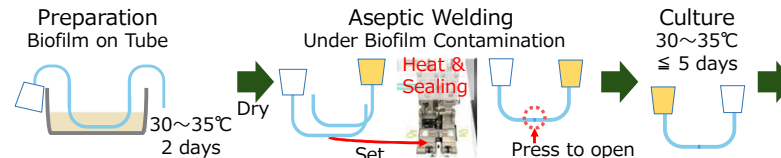
No.	Tube Pattern	Welding device	Microorganism	
			For Spike	For Biofilm
①	Blood Bag Tube - Prodigy Tube	TSCD-II	A <i>Escherichia coli</i>	• <i>Staphylococcus epidermidis</i>
②	Reagent A Tube - Prodigy Tube		B <i>Pseudomonas aeruginosa</i>	
③	Reagent B Tube - Prodigy Tube		C <i>Staphylococcus aureus</i>	
			D <i>Bacillus spizizenii</i>	• <i>Brevundimonas diminuta</i>
			E <i>Candida albicans</i>	

2. Tube connectors

Connectors joined within a liquid phase containing a high concentration of microorganisms.

No.	Connector	Microorganism
④	Connector A	F <i>Brevundimonas diminuta</i>
⑤	Connector B	G <i>Staphylococcus epidermidis</i>
		H <i>Bacillus spizizenii</i>

Legend of Microbial Characteristics
 ● : Gram-positive cocci ● : Spore-forming Gram-positive
 ● : Gram-negative rods ● : Yeast



Results

1. Tube welding device

No.	① Positive (n=3)	② Positive (n=3)	③ Positive (n=3)
A	0	0	0
B	0	0	0
C	0	0	0
D	0	0	0
E	0	0	0

All tests: Negative (no turbidity / no colonies)
 *Photos from a some of the tests

2. Tube connectors

No.	④ Positive (n=3)	⑤ Positive (n=3)	Liquid Phase (CFU/mL)
F	2	3	2.8 × 10 ⁵
G	2	2	3.0 × 10 ⁵
H	1	1	1.0 × 10 ⁵

All conditions: Positive (some of tests: positive)

Conclusions

- **Achievements:** Tube welding device → All sterile under worst-case contamination
 Tube Connectors → Positive cases observed (sterility not assured)
 Sterility assurance requires the use of tube welding devices rather than connectors.
- **Challenges:** Tube combinations differ by device; standardizing sterility assurance remains a challenge.
- **Future:** Expand validation across processes and devices to establish a comprehensive Sterility Assurance Model for closed-system iPS manufacturing.

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